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Interim Recommendations for the Use of *Haemophilius influenzae* Type b (Hib) Conjugate Vaccines Related to the Recall and Recommendations for Increased Surveillance for Vaccine-Associated *Bacillus cereus* Infections

Please distribute to Emergency Departments, Infection Control Departments, Employee Health Services, Infectious Disease Departments, Pediatrics, Family Medicine, Director of Nursing, Medical Director, Pharmacy, Laboratory Director and all patient care areas.

The New York State Department of Health (NYSDOH) and Erie County Department of Health (ECDOH) have been notified of a voluntary recall by Merck & Co. of ten lot numbers of PedvaxHIB® and two lot numbers of COMVAX®. The NYSDOH and ECDOH are providing the information below to providers on the interim recommendations for the use of Hib conjugate vaccines, as the recall is expected to result in short-term disruption to the Hib vaccine supply in the United States. In addition, as part of comprehensive vaccine safety monitoring, the NYSDOH and ECDOH ask that health care providers and clinical laboratories enhance surveillance for vaccine-associated *Bacillus cereus* infections.

1) Interim Recommendations for the Use of *Haemophilus influenzae* Type b (Hib) Conjugate Vaccines Related to the Recall

Merck & Co. has issued a voluntary recall of ten lots of its Pedvax HIB (monovalent Hib vaccine) and two lots of COMVAX (Hib/hepatitis B vaccine) due to concerns about the company's ability to assure sterility for certain specific vaccine lots. Through routine testing of manufacturing equipment, Merck identified the presence of the bacteria Bacillus cereus (B. cereus). Providers who have received affected lots should follow the procedures outlined in the Health Advisory released December 17, 2007. An 11th lot of PedvaxHIB® was also recalled, but it was only used in China. No other U.S. lots of PedvaxHIB® or COMVAX® and no other Merck products are affected by this recall.

- Two other Hib conjugate vaccines manufactured by Sanofi Pasteur, ActHIB® (monovalent Hib vaccine) and TriHIBit® (diphtheria and tetanus toxoids and acellular pertussis [DTaP]/Hib vaccine), are unaffected by the recall and currently available for use in the United States.
    - The vaccines affected by the recall, PedvaxHIB and Comvax, contain Hib capsular polysaccharide (i.e., polyribosylribitol phosphate[PRP]) covalently linked to a meningococcal outer membrane protein (OMP) carrier. PedvaxHIB and Comvax are recommended as a 2-dose primary series at ages 2 and 4 months. PedvaxHIB is also licensed for the 12-15 month booster dose.
    - The two unaffected vaccines, ActHIB and TriHIBit, are polyribosylribitol phosphate-tetanus toxoid (PRP-TT) conjugate Hib vaccines. ActHIB is recommended as a 3-dose primary series at ages 2, 4, and 6 months, and is also licensed for the 12-15 month booster dose. TriHIBit is licensed only for the 12-15 month booster dose.
    - Children who are not at increased risk for Hib disease (described below) and who received PRP-OMP vaccines for only the first or second dose of their routine primary series may be administered PRP-TT to complete the primary series. In these children, a total of 3 doses will complete the primary series. Children who are behind schedule should complete the primary series according to age-appropriate recommendations.
- Because of the short-term reduction in available doses of Hib-containing vaccines, the Centers for Disease Control and Prevention (CDC), in consultation with the Advisory Committee on Immunization Practices (ACIP), the American Academy of Family Physicians, and the American Academy of Pediatrics, recommend that providers temporarily defer administering the routine Hib vaccine booster dose administered at age 12-15 months **except** to children in specific groups at high risk, which are described below. Short-term deferral of the booster dose among children aged 12-15 months is not likely to result in an increased risk for Hib disease.
- Providers should register and track children for whom the booster dose is deferred to facilitate recalling them for vaccination when supplies improve.
- Children at increased risk for Hib disease include children with asplenia, sickle cell disease, human immunodeficiency virus infection and certain other immunodeficiency syndromes, and malignant neoplasms. CDC recommends that providers continue to vaccinate these children with available Hib conjugate vaccines according to the routinely recommended schedules, including the 12-15 month booster dose. PedvaxHIB (if available), ActHIB, and TriHIBit may be used for the booster doses for these children during this shortage.
- Hib vaccines also are recommended for use in prophylaxis for susceptible close contacts of patients with Hib disease. CDC recommends that providers continue to vaccinate close contacts according to published guidelines.
- American Indian/Alaska Native (AI/AN) children also are at increased risk for Hib disease, particularly in the first 6 months of life. Compared with PRP-TT conjugate vaccines, the administration of PRP-OMP vaccines leads to a more rapid seroconversion to protective antibody concentrations within the first 6 months of life. Failure to use PRP-OMP vaccines for the first dose is associated with excess cases of Hib disease in AI/AN infants living in communities where Hib transmission is ongoing and exposure to colonized persons is likely. CDC recommends that providers who currently use PRP-OMP--containing Hib vaccines (PedvaxHIB and Comvax) to serve predominantly AI/AN children in AI/AN communities continue to stock and use only PRP-OMP-- containing Hib vaccines not affected by the recall

and vaccinate according to the routinely recommended schedules, including the 12 -15 month booster dose.

- Limitations of the vaccine supply underscore the importance of surveillance for Hib disease in children and serotyping of *H. influenzae* isolates. ACIP recommends that public health practitioners conduct thorough and timely investigations of all cases of Hib disease. To maximize the amount of available vaccine, providers should order only the number of doses of vaccine required to meet immediate needs (i.e., a supply for up to 4 weeks) and should refrain from attempting to build an inventory of Hib vaccine.

2) Recommendations for Increased Surveillance for Vaccine-Associated *Bacillus cereus* Infections

B. cereus is a common cause of food poisoning. Nongastrointestinal *B. cereus* infections (including wound infections, sepsis, meningoencephalitis, endocarditis, and pneumonia) can occur in persons with compromised immunity or skin barriers. Rarely, cutaneous *B. cereus* infections have been reported in immunocompetent persons. As of December 20, 2007, no cases have been reported to the Vaccine Adverse Event Reporting System (VAERS) of local or disseminated B. cereus infections among children who received vaccines from the affected lots.

As part of comprehensive safety monitoring, CDC and the Food and Drug Administration (FDA) are conducting enhanced surveillance for vaccine-associated B. cereus infections.

- All suspect cases of vaccine-associated *B. cereus* infection should be reported to the local health department (LHD). LHDs should report suspect cases to their NYSDOH Regional Office Immunization Representative.
- A suspect case is defined as infection in any child, aged <6 years, vaccinated in the United States, who: 1) had isolation of *B.cereus* from specimens other than feces or vomitus after any vaccination and 2) had been vaccinated with any vaccine after March 31, 2007.
- All *B. cereus* isolates from suspected cases should be submitted to the NYSDOH Wadsworth Center.

If you have any questions, please contact the ECDOH at 716-858-7697 or the NYSDOH Immunization Program at 518-473-4437.

Attachment 1: CDC. Interim recommendations for the use of *Haemophilus influenzae* type b (Hib) conjugate vaccines related to the recall of certain lots of Hib-containing vaccines (PedvaxHIB® and Comvax®). MMWR Dispatch December 19, 2007; 56:1-2.

Health Category Definitions:

Health Alert FLASH: conveys the highest level of importance due to a large-scale, catastrophic public health emergency; warrants immediate action or attention

Health Alert Priority: conveys the highest level of importance; warrants immediate action or attention to a health problem or situation

Health Advisory: provides important information for a specific incident or situation; may not require immediate action

Health Update: provides updated information regarding an incident or situation; no immediate action necessary

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Interim Recommendations for the Use of *Haemophilus influenzae* Type b (Hib) Conjugate Vaccines Related to the Recall of Certain Lots of Hib-Containing Vaccines (PedvaxHIB® and Comvax®)

On December 13, 2007, Merck & Co., Inc. (West Point, Pennsylvania) announced a voluntary recall of certain lots of two *Haemophilus influenzae* type b (Hib) conjugate vaccines, PedvaxHIB® (monovalent Hib vaccine) and Comvax® (Hib/hepatitis B vaccine). Providers should return unused vaccine from these recalled lots using procedures outlined on the Merck website at http://www.merckvaccines.com/PCHRecall.pdf. Additional information regarding the affected lots is available online from the Food and Drug Administration (FDA) at http://www.fda.gov/consumer/updates/hib121307.html. Merck has suspended production of its Hib conjugate vaccines and does not expect to resume distribution of these vaccines until the fourth quarter of 2008. The recall of PedvaxHIB and Comvax and suspension of production are expected to result in short-term disruption to the Hib vaccine supply in the United States.

Merck issued this voluntary recall as a precautionary measure because the company cannot assure the sterility of equipment used during manufacture of these lots. However, the potency of the vaccine in the recalled lots was not affected, and Merck reported that no contamination of vaccine has been detected. Therefore, children who received Hib conjugate vaccine from the recalled lots do not need revaccination or any special follow-up.

Two other Hib conjugate vaccines manufactured by Sanofi Pasteur (Swiftwater, Pennsylvania) and currently licensed and available for use in the United States, ActHIB® (monovalent Hib vaccine) and TriHIBit® (diphtheria and tetanus toxoids and acellular pertussis [DTaP]/Hib vaccine), are unaffected by the recall. However, Sanofi Pasteur likely will not be able to immediately provide adequate Hib vaccine to vaccinate fully all children for whom the vaccine is recommended (*1*).

The recommended vaccination schedule for all available Hib-containing vaccines consists of a primary series (consisting of 2 or 3 doses, depending on the formulation) administered beginning at age 2 months and a booster dose at age 12–15 months (*1*). Because of the short-term reduction in available doses of Hib-containing vaccines, CDC, in consultation with the Advisory Committee on Immunization Practices (ACIP), the American Academy of Family Physicians, and the American Academy of Pediatrics, recommends that providers temporarily defer administering the routine Hib vaccine booster dose administered at age 12–15 months except to children in specific groups at high risk, which are described in this report. Providers should register and track children for whom the booster dose is deferred to facilitate recalling them for vaccination when supply improves.

Sustained high levels of coverage with Hib conjugate vaccine have resulted in a substantial decline in the incidence of Hib disease in the United States (*2*). In 2006, the incidence of Hib disease in children aged <5 years was 0.21 per 100,000, representing a greater than 99% reduction in disease compared with incidence in the prevaccine era (*3*). Population immunity is a result of direct protection of children by vaccination with Hib vaccine and herd immunity resulting from prevention of nasopharyngeal carriage and interruption of Hib transmission (*4*). Short-term deferral of the booster dose among children aged 12–15 months is not likely to result in an increased risk for Hib disease because of continued protection of children with the primary series and the low level of nasopharyngeal carriage and transmission achieved in the United States by the Hib immunization program.

The vaccines affected by the recall, PedvaxHIB and Comvax, contain Hib capsular polysaccharide (i.e., polyribosylribitol phosphate [PRP]) covalently linked to a meningococcal outer membrane protein (OMP) carrier. The two unaffected vaccines, ActHIB and TriHIBit, are PRP-tetanus toxoid (PRP-TT) conjugate Hib vaccines. PedvaxHIB and Comvax are recommended as a 2-dose primary series (at ages 2 and 4 months), whereas ActHIB is recommended as a 3-dose primary series (at ages 2, 4, and

6 months). ActHIB and PedvaxHIB also are licensed for the 12–15 month booster dose. TriHIBit is licensed only for the 12–15 month booster dose. Children who are not at increased risk for Hib disease, as described in this report, and who received PRP-OMP vaccines for only the first or second dose of their routine primary series may be administered PRP-TT to complete the primary series. In these children, a total of 3 doses will complete the primary series. Children who are behind schedule should complete the primary series according to age-appropriate recommendations (*1*).

Certain children are at increased risk for Hib disease, including children with asplenia, sickle cell disease, human immunodeficiency virus infection and certain other immunodeficiency syndromes, and malignant neoplasms (*5*). CDC recommends that providers continue to vaccinate these children with available Hib conjugate vaccines according to the routinely recommended schedules, including the 12–15 month booster dose. PedvaxHIB (if available), ActHIB, and TriHIBit may be used for the booster doses for these children during this shortage. Hib vaccines also are recommended for use in prophylaxis for susceptible close contacts of patients with Hib disease. CDC recommends that providers continue to vaccinate close contacts according to published guidelines (*5*).

American Indian/Alaska Native (AI/AN) children also are at increased risk for Hib disease, particularly in the first 6 months of life (*5*). Before the use of Hib conjugate vaccines, the incidence of Hib disease among young AI/AN children in AI/AN communities was approximately 10 times higher than among children of comparable age in the general population (*5*). Compared with PRP-TT conjugate vaccines, the administration of PRP-OMP vaccines leads to a more rapid seroconversion to protective antibody concentrations within the first 6 months of life (*6,7*). Failure to use PRP-OMP vaccines for the first dose is associated with excess cases of Hib disease in AI/AN infants living in communities where Hib transmission is ongoing and exposure to colonized persons is likely (*8*). Although PRP-OMP and PRP-TT vaccines are equally effective after completion of the primary series, availability of more than one Hib vaccine in a clinic could lead to administration of the wrong vaccine for the first dose in these populations (*5*). For these reasons, CDC recommends that providers who currently use PRP-OMP–containing Hib vaccines (PedvaxHIB and Comvax) to serve predominantly AI/AN children in AI/AN communities continue to stock and use only PRP-OMP– containing Hib vaccines not affected by the recall and vaccinate according to the routinely recommended schedules, including the 12–15 month booster dose. In its vaccine stockpile, CDC has PRP-OMP–containing Hib vaccines not affected by the recall and will prioritize distribution of available PRP-OMP vaccines for use in AI/AN communities. AI/AN children not in AI/AN communities or who already receive PRP-TT conjugate vaccines should continue to be vaccinated with available vaccines according to the routinely recommended schedules, including the 12–15 month booster dose.

Limitations of the vaccine supply underscore the importance of surveillance for Hib disease in children and serotyping of *H. influenzae* isolates. ACIP recommends that public health practitioners conduct thorough and timely investigations of all cases of Hib disease. To maximize the amount of available vaccine, providers should order only the number of doses of vaccine required to meet immediate needs (i.e., a supply for up to 4 weeks) and should refrain from attempting to build an inventory of Hib vaccine. CDC, ACIP, and other partners will continue to monitor the supply of available Hib vaccines and the epidemiology of Hib disease and provide updates when available. FDA and CDC will continue to monitor the safety of Hib vaccines. Any adverse events that are potentially vaccine-related should be reported to the Vaccine Adverse Event Reporting System (VAERS) by telephone (800-822-7967) or online (http://www.vaers.hhs.gov). Additional information regarding Hib vaccine is available at http://www.cdc.gov/vaccines/vpd-vac/hib/default.htm. Updates on vaccine supply are available at http://www.cdc.gov/vaccines/vac-gen/shortages/default.htm#chart.

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